EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S1	651	EDG REceptor	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	AND	ON	2007/07/03 12:46
S2	15	(Endothelial ADJ differentiation ADJ gene ADJ REceptor) AND @ad<="20021212"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	AND	ON	2007/05/03 19:31
S3	47	(Lysophosphatidic acid (LPA) receptor) SAME (agonists OR antagonists) AND @ad<="20031211"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	AND	ON	2007/07/03 14:20

```
Connecting via Winsock to STN


Welcome to STN International!  Enter x:x

LOGINID:SSPTAEGS1646

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1           Web Page for STN Seminar Schedule - N. America
 NEWS  2  MAR 15   WPIDS/WPIX enhanced with new FRAGHITSTR display format
 NEWS  3  MAR 16   CASREACT coverage extended
 NEWS  4  MAR 20   MARPAT now updated daily
 NEWS  5  MAR 22   LWPI reloaded
 NEWS  6  MAR 30   RDISCLOSURE reloaded with enhancements
 NEWS  7  APR 02   JICST-EPLUS removed from database clusters and STN
 NEWS  8  APR 30   GENBANK reloaded and enhanced with Genome Project ID field
 NEWS  9  APR 30   CHEMCATS enhanced with 1.2 million new records
 NEWS 10  APR 30   CA/CAplus enhanced with 1870-1889 U.S. patent records
 NEWS 11  APR 30   INPADOC replaced by INPADOCDB on STN
 NEWS 12  MAY 01   New CAS web site launched
 NEWS 13  MAY 08   CA/CAplus Indian patent publication number format defined
 NEWS 14  MAY 14   RDISCLOSURE on STN Easy enhanced with new search and display
                   fields
 NEWS 15  MAY 21   BIOSIS reloaded and enhanced with archival data
 NEWS 16  MAY 21   TOXCENTER enhanced with BIOSIS reload
 NEWS 17  MAY 21   CA/CAplus enhanced with additional kind codes for German
                   patents
 NEWS 18  MAY 22   CA/CAplus enhanced with IPC reclassification in Japanese
                   patents
 NEWS 19  JUN 27   CA/CAplus enhanced with pre-1967 CAS Registry Numbers
 NEWS 20  JUN 29   STN Viewer now available
 NEWS 21  JUN 29   STN Express, Version 8.2, now available
 NEWS 22  JUL 02   LEMBASE coverage updated
 NEWS 23  JUL 02   LMEDLINE coverage updated
 NEWS 24  JUL 02   SCISEARCH enhanced with complete author names
 NEWS 25  JUL 02   CHEMCATS accession numbers revised
 NEWS 26  JUL 02   CA/CAplus enhanced with utility model patents from China

 NEWS EXPRESS  29 JUNE 2007:  CURRENT WINDOWS VERSION IS V8.2,
               CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 4 MAY 2007.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *
```

```
FILE 'HOME' ENTERED AT 09:45:37 ON 03 JUL 2007

=> File .gerry2MBCE
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'MEDLINE' ENTERED AT 09:45:58 ON 03 JUL 2007

FILE 'BIOSIS' ENTERED AT 09:45:58 ON 03 JUL 2007
Copyright (c) 2007 The Thomson Corporation

FILE 'CAPLUS' ENTERED AT 09:45:58 ON 03 JUL 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'EMBASE' ENTERED AT 09:45:58 ON 03 JUL 2007
Copyright (c) 2007 Elsevier B.V. All rights reserved.

=> S Nephropathy
L1      108930 NEPHROPATHY

=> Dup Rem L1
108930 ANSWERS REQUESTED EXCEEDS MAXIMUM ALLOWED OF 50000
You may process up to 50,000 answers per command.  Please try to
narrow your search until your resulting L# answer set is within the
maximum number of answers.

=> S lysophosphatidic acid
L2       10068 LYSOPHOSPHATIDIC ACID

=> S EDG receptor
L3         419 EDG RECEPTOR

=> S L1 AND L2 AND L3
L4           0 L1 AND L2 AND L3

=> S L2 AND l3
L5         190 L2 AND L3

=> Dup Rem l5
PROCESSING COMPLETED FOR L5
L6           87 DUP REM L5 (103 DUPLICATES REMOVED)
                ANSWERS '1-39' FROM FILE MEDLINE
                ANSWERS '40-62' FROM FILE BIOSIS
                ANSWERS '63-82' FROM FILE CAPLUS
                ANSWERS '83-87' FROM FILE EMBASE

=> S L6 AND Therapy
L7           4 L6 AND THERAPY

=> D ti L7 1-4

L7   ANSWER 1 OF 4     MEDLINE on STN
TI   EDG receptors as a potential therapeutic target in
     retinal ischemia-reperfusion injury.

L7   ANSWER 2 OF 4     MEDLINE on STN
TI   Critical role of lysophospholipids in the pathophysiology, diagnosis, and
     management of ovarian cancer.

L7   ANSWER 3 OF 4  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
TI   EDG receptors as a therapeutic target in retinal
     ischemic injury.
```

L7 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
TI Lysophosphatidic acid is a bioactive mediator in ovarian cancer

=> D ibib abs L7 1-4

L7 ANSWER 1 OF 4 MEDLINE on STN
ACCESSION NUMBER: 2006707700 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17026968
TITLE: EDG receptors as a potential therapeutic target in retinal ischemia-reperfusion injury.
AUTHOR: Savitz Sean I; Dhallu Manjeet S; Malhotra Samit; Mammis Antonios; Ocava Lenore C; Rosenbaum Pearl S; Rosenbaum Daniel M
CORPORATE SOURCE: Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, USA.. drosenba@aecom.yu.edu
CONTRACT NUMBER: EY11257 (NEI)
EY1253 (NEI)
SOURCE: Brain research, (2006 Nov 6) Vol. 1118, No. 1, pp. 168-75. Electronic Publication: 2006-10-05. Journal code: 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, N.I.H., EXTRAMURAL) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200701
ENTRY DATE: Entered STN: 6 Dec 2006 Last Updated on STN: 24 Jan 2007 Entered Medline: 23 Jan 2007
AB LPA (lysophosphatidic acid) specific endothelial differentiation gene (EDG) receptors have been implicated in various anti-apoptotic pathways. Ischemia of the brain and retina causes neuronal apoptosis, which raises the possibility that EDG receptors participate in anti-apoptotic signaling in ischemic injury. We examined the expression of EDG receptors in a model of retinal ischemia-reperfusion injury and also tested LXR-1035, a novel analogue of LPA, in the rat following global retinal ischemic injury. Rats were subjected to 45 or 60 min of raised intraocular pressure. Animals were sacrificed at 24 h post-ischemia and retinal tissue was stained for EDG receptors. In separate experiments, animals were randomized to receive LXR or saline vehicle by intravitreal injection 24 h prior to ischemia. The degree of retinal damage was assessed morphologically by measuring the thickness of the inner retinal layers as well as functionally by electroretinography (ERG). We found that the normal retina has a baseline expression of the LPA receptors, EDG-2 and EDG-4, which are significantly upregulated in the inner layers in response to ischemia. Animals pretreated with LXR-1035 had dose-dependent, significant reductions in histopathologic damage and significant improvement in functional deficits compared with corresponding vehicle-controls, after 45 and 60 min of ischemia. These results suggest that LPA receptor signaling may play an important role in neuroprotection in retinal ischemia-reperfusion injury.

L7 ANSWER 2 OF 4 MEDLINE on STN
ACCESSION NUMBER: 2002047383 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11775454
TITLE: Critical role of lysophospholipids in the pathophysiology, diagnosis, and management of ovarian cancer.
AUTHOR: Mills Gordon B; Eder Astrid; Fang Xianjun; Hasegawa Yutaka; Mao Muling; Lu Yiling; Tanyi Janos; Tabassam Fazal Haq; Wiener Jon; Lapushin Ruth; Yu Shiangxing; Parrott Jeff A;

Compton Tim; Tribley Walter; Fishman David; Stack M Sharon; Gaudette Douglas; Jaffe Robert; Furui Tatsuro; Aoki Junken; Erickson James R

CORPORATE SOURCE: Department of Molecular Therapeutics, MD Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, Texas 77030, USA.

CONTRACT NUMBER: P01 CA64602 (NCI)
SOURCE: Cancer treatment and research, (2002) Vol. 107, pp. 259-83.
Ref: 89
Journal code: 8008541. ISSN: 0927-3042.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 25 Jan 2002
Last Updated on STN: 24 Apr 2002
Entered Medline: 23 Apr 2002

AB Lysophosphatidic acid (LPA), the simplest of all phospholipids, exhibits pleiomorphic functions in multiple cell lineages. The effects of LPA appear to be mediated by binding of LPA to specific members of the endothelial differentiation gene (Edg) family of G protein-coupled receptors (GPCR). Edg 2, Edg4, and Edg7 are high affinity receptors for LPA, and Edg1 may be a low affinity receptor for LPA. PSP24 has been shown to be responsive to LPA in Xenopus oocytes, however, its role in mammalian cells is unclear. The specific biochemical events initiated by the different Edg receptors, as well as the biological outcomes of activation of the individual receptors, are only beginning to be determined. LPA levels are consistently elevated in the plasma and ascites of ovarian cancer patients, but not in most other epithelial tumors, with the exception of cervix and endometrium, suggesting that LPA may be of particular importance in the pathophysiology of ovarian cancer. In support of this concept, ovarian cancer cells constitutively and inducibly produce high levels of LPA and demonstrate markedly different responses to LPA than normal ovarian surface epithelium. Edg4 and Edg7 levels are consistently increased in malignant ovarian epithelial cells contributing to the aberrant response of ovarian cancer cells to LPA. Edg2 may represent a negative regulatory LPA receptor inducing apoptosis in ovarian cancer cells. Thus, increased levels of LPA, altered receptor expression and altered responses to LPA may contribute to the initiation, progression or outcome of ovarian cancer. Over 40% of known drugs target GPCR, making LPA receptors attractive targets for molecular therapeutics. Indeed, using the structure-function relationship of LPA in model systems, we have identified selective Edg2 anatgonists, as well as Edg4 and Edg7 agonists. These lead compounds are being assessed in preclinical model systems. Understanding the mechanisms regulating LPA production, metabolism and function could lead to improved methods for early detection and to new targets for therapy in ovarian cancer.

L7 ANSWER 3 OF 4 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2006:47950 BIOSIS
DOCUMENT NUMBER: PREV200600057152

TITLE: EDG receptors as a therapeutic target in retinal ischemic injury.

AUTHOR(S): Rosenbaum, D. M. [Reprint Author]; Singh, M.; Malhotra, S.; Savitz, S. I.; Ocava, L. C.; Rosenbaum, P. S.

SOURCE: IOVS, (2005) Vol. 46, No. Suppl. S, pp. 5316.
Meeting Info.: Annual Meeting of the Association-for-Research-in-Vision-and-Ophthalmology. Ft Lauderdale, FL, USA. May 01 -05, 2005. Assoc Res Vis & Ophthalmol.
CODEN: IOVSDA. ISSN: 0146-0404.
DOCUMENT TYPE: Conference; (Meeting)

Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Jan 2006
Last Updated on STN: 4 Jan 2006

AB Purpose: EDG receptors are a family of G-protein coupled receptors that play an important role in cell growth, development and maintenance, survival and cytoskeletal changes. They exert their effect via intracellular signaling pathways involving various kinases. The purpose of this study was to evaluate the role of lysophosphatidic acid (LPA) -specific EDG receptors (EDG-2 and EDG-4) as therapeutic targets in a model of retinal ischemia. Methods: Transient retinalischemia was induced in Sprague-Dawley rats by increasing the intraocular pressure above systolic arterial pressure(HIOP) for 45 minutes. Immunohistochemistry for EDG receptor was performed at different times following reperfusion. In a separate set of experiments, intravitreal injections of a novel analog of LPA, LXR 1035, was given 6 hours before and 5 minutes after ischemia (HIOP). These animals were sacrificed at 7 days and retinal tissue harvested to evaluate retinal thickness and cell counts. Retinal function was evaluated by electroretinograms (ERG's). Results: EDG-2 and EDG-4 receptor staining was maximally evident at 24 hours following ischemia in the ganglion cell layer and the inner nuclear layer as compared to the sham group of animals where no staining was noted. The LXR 1035-treated group of animals showed significant preservation of retinal thickness, cell counts and retinal function as compared to the vehicle-treated group of animals. Conclusions: The neuroprotective effect of EDGreceptors in retinal ischemia-reperfusion maybe mediated via activation of phosphatidylinositol 3-kinase, Akt and MAPK and inhibiting cyclic AMP production. Therapies aimed at manipulating these receptors offers potential targets fortherapeutic strategies for ischemic retinal disorders.

L7 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:459270 CAPLUS
DOCUMENT NUMBER: 137:199096
TITLE: Lysophosphatidic acid is a bioactive mediator in ovarian cancer
AUTHOR(S): Fang, Xianjun; Schummer, Michel; Mao, Muling; Yu, Shuangxing; Tabassam, Fazal Haq; Swaby, Ramona; Hasegawa, Yutaka; Tanyi, Janos L.; LaPushin, Ruthie; Eder, Astrid; Jaffe, Robert; Erickson, Jim; Mills, Gordon B.
CORPORATE SOURCE: Department of Molecular Therapeutics, University of Texas M.D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Biochimica et Biophysica Acta, Molecular and Cell Biology of Lipids (2002), 1582(1-3), 257-264
CODEN: BBMLFG; ISSN: 1388-1981
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Lysophosphatidic acid (LPA) is a naturally occurring phospholipid that exhibits pleiotrophic biol. activities, ranging from rapid morphol. changes to long-term cellular effects such as induction of gene expression and stimulation of cell proliferation and survival on a wide spectrum of cell types. LPA binds and activates distinct members of the Edg/LP subfamily of G protein-coupled receptors that link to multiple G proteins including G(i), G(q) and G(12/13) to elicit cellular responses. LPA plays a critical role as a general growth, survival and pro-angiogenic factor, in the regulation of physiol. and pathophysiol. processes in vivo and in vitro. Our previous work indicates that abnormalities in LPA metabolism and function in ovarian cancer patients may contribute to the initiation and progression of the disease. Thus, LPA could be a potential target for cancer therapy. This review summarizes evidence that implicates LPA in the pathophysiol. of human

```
     ovarian cancer and likely other types of human malignancies.
REFERENCE COUNT:         68    THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> Log off H
 SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 09:50:52 ON 03 JUL 2007

Connecting via Winsock to STN



Welcome to STN International!  Enter x:x

LOGINID:SSPTAEGS1646

PASSWORD:
 * * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE'
AT 11:08:04 ON 03 JUL 2007
FILE 'MEDLINE' ENTERED AT 11:08:04 ON 03 JUL 2007
FILE 'BIOSIS' ENTERED AT 11:08:04 ON 03 JUL 2007
Copyright (c) 2007 The Thomson Corporation
FILE 'CAPLUS' ENTERED AT 11:08:04 ON 03 JUL 2007
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)
FILE 'EMBASE' ENTERED AT 11:08:04 ON 03 JUL 2007
Copyright (c) 2007 Elsevier B.V. All rights reserved.

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      24.49      24.70

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                      -0.78      -0.78

=> D Hist

     (FILE 'HOME' ENTERED AT 09:45:37 ON 03 JUL 2007)

     FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 09:45:58 ON 03 JUL 2007
L1       108930 S NEPHROPATHY
L2        10068 S LYSOPHOSPHATIDIC ACID
L3          419 S EDG RECEPTOR
L4            0 S L1 AND L2 AND L3
L5          190 S L2 AND L3
L6           87 DUP REM L5 (103 DUPLICATES REMOVED)
L7            4 S L6 AND THERAPY

=> S L6 AND modulator
L8            4 L6 AND MODULATOR

=> D Ti L8 1-4

L8   ANSWER 1 OF 4     MEDLINE on STN
TI   Native and recombinant human Edg4 receptor-mediated Ca(2+) signalling.

L8   ANSWER 2 OF 4  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Screening for substituted aryl isoxazole effectors of the Edg-1 receptor
     for the treatment of receptor-associated conditions

L8   ANSWER 3 OF 4  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Modulators of EDG receptors, LPA receptors,
```

and S1P receptors for the modulation of neural stem cells and neural progenitor cells and treatment of nervous system disorders

L8 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
TI Methods using Edg receptor modulators for the treatment of Edg receptor-associated conditions

=> D Ibib Abs 1-4

L8 ANSWER 1 OF 4 MEDLINE on STN
ACCESSION NUMBER: 2004193628 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15090154
TITLE: Native and recombinant human Edg4 receptor-mediated Ca(2+) signalling.
AUTHOR: Simpson Peter B; Villullas Israel Ramos; Schurov Irina; Kerby Julie; Millard Rachel; Haldon Christine; Beer Margaret S; McAllister George
CORPORATE SOURCE: Merck Sharp & Dohme Research Laboratories, Neuroscience Research Centre, Harlow, Essex, UK.. peter_simpson@merck.com
SOURCE: Assay and drug development technologies, (2002 Nov) Vol. 1, No. 1 Pt 1, pp. 31-40.
Journal code: 101151468. ISSN: 1540-658X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 20 Apr 2004
Last Updated on STN: 20 May 2004
Entered Medline: 19 May 2004
AB We have developed an assay system suitable for assessment of compound action on the Edg4 subtype of the widely expressed lysophosphatidic acid (LPA)-responsive Edg receptor family. Edg4 was stably overexpressed in the rat hepatoma cell line Rh 7777, and a Ca(2+)-based FLIPR assay developed for measurement of functional responses. In order to investigate the mechanisms linking Edg4 activation to cytosolic Ca(2+) elevation, we have also studied LPA signalling in a human neuroblastoma cell line that endogenously expresses Edg4. LPA responses displayed similar kinetics and potency in the two cell lines. The Ca(2+) signal generated by activation of LPA-sensitive receptors in these cells is mediated primarily by endoplasmic reticulum. However, there is a substantial inhibition of the LPA response by FCCP, indicating that mitochondria also play a key role in the LPA response. Partial inhibition of the response by cyclosporin A could indicate an active Ca(2+) release role for mitochondria in the LPA response. The inositol 1,4,5-triphosphate receptor antagonist 2-aminoethyl diphenyl borate markedly inhibits, but does not abolish, the Ca(2+) response to LPA, suggesting further complexity to the signalling pathways activated by Edg receptors. In comparing Edg signalling in recombinant and native cells, there is a striking overall similarity in receptor expression pattern, agonist potency, and the effect of modulators on the Ca(2+) response. This indicates that the Edg4-overexpressing Rh7777 cell line is a very useful model system for studying receptor pharmacology and signalling mechanisms, and for investigating the Edg4 receptor's downstream effects.

L8 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:80878 CAPLUS
DOCUMENT NUMBER: 140:139547
TITLE: Screening for substituted aryl isoxazole effectors of the Edg-1 receptor for the treatment of receptor-associated conditions
INVENTOR(S): Solow-Cordero, David; Shankar, Geetha; Gluchowski,

Charles; Spencer, Juliet V.
PATENT ASSIGNEE(S): Ceretek Llc, USA
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004009816	A1	20040129	WO 2003-US22463		20030717
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2466288	A1	20040129	CA 2003-2466288		20030717
AU 2003252023	A1	20040209	AU 2003-252023		20030717
US 2004147562	A1	20040729	US 2003-621966		20030717
EP 1523556	A1	20050420	EP 2003-765716		20030717
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2005533852	T	20051110	JP 2004-523557		20030717
PRIORITY APPLN. INFO.:			US 2002-397299P	P	20020718
			WO 2003-US22463	W	20030717

OTHER SOURCE(S): MARPAT 140:139547
AB In one aspect, the present invention provides a method of modulating an Edg-1 receptor mediated biol. activity in a cell. A cell expressing the Edg-1 receptor is contacted with a modulator of the Edg-1 receptor sufficient to modulate the Edg-1 receptor mediated biol. activity. In another aspect, the present invention provides a method for modulating an Edg-1 receptor mediated biol. activity in a subject. A therapeutically effective amount of a modulator of the Edg-1 receptor is administered to the subject.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:913038 CAPLUS
DOCUMENT NUMBER: 139:375041
TITLE: Modulators of EDG receptors, LPA receptors, and S1P receptors for the modulation of neural stem cells and neural progenitor cells and treatment of nervous system disorders
INVENTOR(S): Lindquist, Per; Mercer, Alex; Ronnholm, Harriet; Wikstrom, Lilian
PATENT ASSIGNEE(S): Neuronova A.B., Swed.
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003094965	A2	20031120	WO 2003-IB2370	20030508
WO 2003094965	A3	20040722		

WO 2003094965 A8 20040826
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003233119	A1	20031111	AU 2003-233119	20030508
US 2004014662	A1	20040122	US 2003-434943	20030508
PRIORITY APPLN. INFO.:			US 2002-379114P	P 20020508
			US 2002-393159P	P 20020702
			WO 2003-IB2370	W 20030508

AB The invention discloses methods of influencing central nervous system cells to produce progeny useful in the treatment of CNS disorders. More specifically, the invention includes methods of exposing a patient suffering from such a disorder to a reagent that modulates the proliferation, migration, differentiation and survival of central nervous system cells via sphingosine-1-phosphate (S1P) or lysophosphatidic acid (LPA) signaling. These methods are useful for reducing at least one symptom of the disorder. The methodol. of the invention uses modulators of S1P, LPA, or EDG receptors.

L8 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2003:591307 CAPLUS
DOCUMENT NUMBER:	139:143997
TITLE:	Methods using Edg receptor modulators for the treatment of Edg receptor-associated conditions
INVENTOR(S):	Shankar, Geetha; Solow-Cordero, David; Spencer, Juliet V.; Gluchowski, Charles
PATENT ASSIGNEE(S):	Ceretek LLC, USA
SOURCE:	PCT Int. Appl., 293 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003062392	A2	20030731	WO 2003-US1881	20030121
WO 2003062392	A3	20050120		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2473740	A1	20030731	CA 2003-2473740	20030121
AU 2003214873	A1	20030902	AU 2003-214873	20030121
EP 1513522	A2	20050316	EP 2003-710713	20030121

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

JP 2005519915	T	20050707	JP 2003-562260	20030121
US 2005261298	A1	20051124	US 2003-390428	20030314
PRIORITY APPLN. INFO.:			US 2002-350445P	P 20020118
			US 2002-350446P	P 20020118

```
                                                US 2002-350447P      P  20020118
                                                US 2002-350448P      P  20020118
                                                WO 2003-US1881       W  20030121
                                                US 2003-352579       B2 20030127
OTHER SOURCE(S):          MARPAT 139:143997
AB   The invention provides a method of modulating an Edg-2, Edg-3, Ed-4 or
     Edg7 receptor-mediated biol. activity in a cell.  A cell expressing the
     Edg-2, Edg-3, Edg-4 or Edg 7 receptor is contacted with a
     modulator of the Edg-2, Edg-3, Ed-4 or Edg 7 receptor sufficient
     to modulate receptor mediated biol. activity.  In another aspect, the
     present invention provides a method for modulating an Edg-2, Edg-3, Ed-4
     or Edg-7 receptor mediated biol. in a subject.  A therapeutically
     effective amount of a modulator of the Edg-2, Edg-3, Ed-4 or Edg7
     receptor is administered to the subject.  Preparation of compds., e.g.
     4,4,4-trifluoro-3-oxo-N-(5-phenyl-2H-pyrazol-3-yl)butyramide, is
     described.


=> D Hist

     (FILE 'HOME' ENTERED AT 09:45:37 ON 03 JUL 2007)

     FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 09:45:58 ON 03 JUL 2007
L1        108930 S NEPHROPATHY
L2         10068 S LYSOPHOSPHATIDIC ACID
L3           419 S EDG RECEPTOR
L4             0 S L1 AND L2 AND L3
L5           190 S L2 AND L3
L6            87 DUP REM L5 (103 DUPLICATES REMOVED)
L7             4 S L6 AND THERAPY
L8             4 S L6 AND MODULATOR

=> S L2 (S)(agonist OR Analog OR antagonist OR Inhibitor)
L9         1072 L2 (S)(AGONIST OR ANALOG OR ANTAGONIST OR INHIBITOR)

=> S L9 AND pd<=20031211
   2 FILES SEARCHED...
L10         695 L9 AND PD<=20031211

=> Dup rem L10
PROCESSING COMPLETED FOR L10
L11          303 DUP REM L10 (392 DUPLICATES REMOVED)
                 ANSWERS '1-144' FROM FILE MEDLINE
                 ANSWERS '145-200' FROM FILE BIOSIS
                 ANSWERS '201-292' FROM FILE CAPLUS
                 ANSWERS '293-303' FROM FILE EMBASE

=> S L11 (S)(EDG-2 OR EDG2 OR LPA1)
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L56 (S)(EDG-2'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L58 (S)(EDG-2'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L60 (S)(EDG-2'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L62 (S)(EDG-2'
L12          37 L11 (S)(EDG-2 OR EDG2 OR LPA1)

=> D ti L12 1-37

L12  ANSWER 1 OF 37     MEDLINE on STN
TI   Cyclic phosphatidic acid elicits neurotrophin-like actions in embryonic
     hippocampal neurons.

L12  ANSWER 2 OF 37     MEDLINE on STN
```

TI Pharmacological characterization of lysophospholipid receptor signal transduction pathways in rat cerebrocortical astrocytes.

L12 ANSWER 3 OF 37 MEDLINE on STN
TI Ki16425, a subtype-selective antagonist for EDG-family lysophosphatidic acid receptors.

L12 ANSWER 4 OF 37 MEDLINE on STN
TI Subtype-selective antagonists of lysophosphatidic Acid receptors inhibit platelet activation triggered by the lipid core of atherosclerotic plaques.

L12 ANSWER 5 OF 37 MEDLINE on STN
TI Agonist-induced endocytosis of lysophosphatidic acid-coupled LPA1/EDG-2 receptors via a dynamin2- and Rab5-dependent pathway.

L12 ANSWER 6 OF 37 MEDLINE on STN
TI Human platelets respond differentially to lysophosphatidic acids having a highly unsaturated fatty acyl group and alkyl ether-linked lysophosphatidic acids.

L12 ANSWER 7 OF 37 MEDLINE on STN
TI Molecular basis for lysophosphatidic acid receptor antagonist selectivity.

L12 ANSWER 8 OF 37 MEDLINE on STN
TI Noradrenaline release-inhibiting receptors on PC12 cells devoid of alpha(2(-)) and CB(1) receptors: similarities to presynaptic imidazoline and edg receptors.

L12 ANSWER 9 OF 37 MEDLINE on STN
TI Activity of 2-substituted lysophosphatidic acid (LPA) analogs at LPA receptors: discovery of a LPA1/LPA3 receptor antagonist.

L12 ANSWER 10 OF 37 MEDLINE on STN
TI Identification of lysophospholipid receptors in human platelets: the relation of two agonists, lysophosphatidic acid and sphingosine 1-phosphate.

L12 ANSWER 11 OF 37 MEDLINE on STN
TI Naturally occurring analogs of lysophosphatidic acid elicit different cellular responses through selective activation of multiple receptor subtypes.

L12 ANSWER 12 OF 37 MEDLINE on STN
TI Edg-2/Vzg-1 couples to the yeast pheromone response pathway selectively in response to lysophosphatidic acid.

L12 ANSWER 13 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Lack of stereospecificity in lysophosphatidic acid enantiomer-induced calcium mobilization in human erythroleukemia cells.

L12 ANSWER 14 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI LYSOPHOSPHATIDIC ACID IS A GROWTH FACTOR FOR HEPATIC OVAL (STEM) CELLS.

L12 ANSWER 15 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI CHARACTERIZATION OF LYSOPHOSPHOLIPID RECEPTOR (LPR) SIGNAL TRANSDUCTION PATHWAYS IN RAT CORTICAL ASTROCYTES (AST).

L12 ANSWER 16 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on

STN
TI Lysophosphatidic acid (LPA) regulation of murine blastocyst development involves crosstalk with embryonic heparin-binding epidermal growth factor-like growth factor (HB-EGF).

L12 ANSWER 17 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Fatty alcohol phosphates are subtype-selective agonists and antagonists of lysophosphatidic acid receptors.

L12 ANSWER 18 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI A dual lysophosphatidic acid (LPA) antagonist (LPA1/LPA3), VPC 12249, reduces renal ischemia-reperfusion injury (IRI).

L12 ANSWER 19 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Stereochemical properties of lysophosphatidic acid receptor activation and metabolism.

L12 ANSWER 20 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Lysophosphatidic acid (LPA) induced hypertrophy in rat neonatal myocytes.

L12 ANSWER 21 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI LPA analogs as agonists of the Edg2 LPA receptor.

L12 ANSWER 22 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Agonist-induced internalization of lysophosphatidic acid-coupled Edg2 receptors via clathrin-dependent endocytosis.

L12 ANSWER 23 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of N-(2'-carbamoyl-1,1'-biphenyl-2-ylcarbonyl)-β-alanine derivatives as lysophosphatidic acid receptor antagonists

L12 ANSWER 24 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Lysophosphatidic acid (LPA) receptor agonists and antagonists, their preparation, and methods of use

L12 ANSWER 25 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Identification of p2y9/GPR23 as a Novel G Protein-coupled Receptor for Lysophosphatidic Acid, Structurally Distant from the Edg Family

L12 ANSWER 26 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Lysophosphatidic acid (LPA) receptor agonists and antagonists, their preparation, and methods of use

L12 ANSWER 27 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Synthesis and biological evaluation of lysophosphatidic acid antagonists

L12 ANSWER 28 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Molecular modeling of lysophosphatidic acid receptor antagonists

L12 ANSWER 29 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Novel lysophosphatidic acid receptor agonists and antagonists

L12 ANSWER 30 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Role of ether-linked lysophosphatidic acids in ovarian cancer cells

L12 ANSWER 31 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Synthesis of lysophosphatidic acid receptor agonists and antagonists and their use for cancer inhibition, wound healing, and enhancement of cell proliferation

L12 ANSWER 32 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Assessment of agonism at G-protein coupled receptors by phosphatidic acid and lysophosphatidic acid in human embryonic kidney 293 cells

L12 ANSWER 33 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Methods for detecting compounds which modulate the activity of LPA (lysophosphatidic acid) and its receptor EDG-2

L12 ANSWER 34 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Lysophosphatidic acid (LPA) receptors of the EDG family are differentially activated by LPA species. Structure-activity relationship of cloned LPA receptors

L12 ANSWER 35 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Analysis of the EDG2 receptor based on the structure/activity relationship of LPA

L12 ANSWER 36 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Methods using a lysophosphatidic acid receptor agonist for promoting survival of myelin-producing cells

L12 ANSWER 37 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Recombinant human G protein-coupled lysophosphatidic acid receptors mediate intracellular calcium mobilization

=> Log off H
SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 11:17:22 ON 03 JUL 2007

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAEGS1646

PASSWORD:
* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE'
AT 11:22:07 ON 03 JUL 2007
FILE 'MEDLINE' ENTERED AT 11:22:07 ON 03 JUL 2007
FILE 'BIOSIS' ENTERED AT 11:22:07 ON 03 JUL 2007
Copyright (c) 2007 The Thomson Corporation
FILE 'CAPLUS' ENTERED AT 11:22:07 ON 03 JUL 2007
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)
FILE 'EMBASE' ENTERED AT 11:22:07 ON 03 JUL 2007
Copyright (c) 2007 Elsevier B.V. All rights reserved.

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	69.83	70.04

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION

```
CA SUBSCRIBER PRICE                                    -3.12       -3.12

=> D Hist

     (FILE 'HOME' ENTERED AT 09:45:37 ON 03 JUL 2007)

     FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 09:45:58 ON 03 JUL 2007
L1        108930 S NEPHROPATHY
L2         10068 S LYSOPHOSPHATIDIC ACID
L3           419 S EDG RECEPTOR
L4             0 S L1 AND L2 AND L3
L5           190 S L2 AND L3
L6            87 DUP REM L5 (103 DUPLICATES REMOVED)
L7             4 S L6 AND THERAPY
L8             4 S L6 AND MODULATOR
L9          1072 S L2 (S)(AGONIST OR ANALOG OR ANTAGONIST OR INHIBITOR)
L10          695 S L9 AND PD<=20031211
L11          303 DUP REM L10 (392 DUPLICATES REMOVED)
L12           37 S L11 (S)(EDG-2 OR EDG2 OR LPA1)

=> D Ibib Abs L12 18

L12  ANSWER 18 OF 37  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on
     STN
ACCESSION NUMBER:    2002:567555  BIOSIS
DOCUMENT NUMBER:     PREV200200567555
TITLE:               A dual lysophosphatidic acid (LPA)
                     antagonist (LPA1/LPA3), VPC 12249,
                     reduces renal ischemia-reperfusion injury (IRI).
AUTHOR(S):           Okusa, Mark D. [Reprint author]; Ye, Hong [Reprint author];
                     Huang, Liping [Reprint author]; Heise, Christopher E.;
                     Santos, Webster L.; MacDonald, Timonthy; Lynch, Kevin R.
CORPORATE SOURCE:    Medicine, University of Virginia, Charlottesville, VA, USA
SOURCE:              Journal of the American Society of Nephrology, (
                     September, 2002) Vol. 13, No. Program and Abstracts
                     Issue, pp. 140A. print.
                     Meeting Info.: Meeting of the American Society of
                     Nephrology. Philadelphia, PA, USA. October 30-November 04,
                     2002. American Society of Nephrology.
                     CODEN: JASNEU. ISSN: 1046-6673.
DOCUMENT TYPE:       Conference; (Meeting)
                     Conference; Abstract; (Meeting Abstract)
LANGUAGE:            English
ENTRY DATE:          Entered STN: 7 Nov 2002
                     Last Updated on STN: 7 Nov 2002


=> FIL STNGUIDE
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY     SESSION
FULL ESTIMATED COST                                    74.35       74.56

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                      ENTRY     SESSION
CA SUBSCRIBER PRICE                                    -3.12       -3.12

FILE 'STNGUIDE' ENTERED AT 11:23:39 ON 03 JUL 2007
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Jun 29, 2007 (20070629/UP).

=> D Ibib ABS L12 11, 17,21-24,26,27,29,31,32
YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE, BIOSIS, CAPLUS' - CONTINUE? (Y)/N:y
```

L12 ANSWER 11 OF 37 MEDLINE on STN
ACCESSION NUMBER: 1999074344 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9855625
TITLE: Naturally occurring analogs of lysophosphatidic acid elicit different cellular responses through selective activation of multiple receptor subtypes.
AUTHOR: Fischer D J; Liliom K; Guo Z; Nusser N; Virag T; Murakami-Murofushi K; Kobayashi S; Erickson J R; Sun G; Miller D D; Tigyi G
CORPORATE SOURCE: Department of Physiology and Biophysics, The University of Tennessee, Memphis, TN 38163, USA.
CONTRACT NUMBER: HL07746 (NHLBI)
SOURCE: Molecular pharmacology, (1998 Dec) Vol. 54, No. 6, pp. 979-88.
Journal code: 0035623. ISSN: 0026-895X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 28 Jan 1999
Last Updated on STN: 28 Jan 1999
Entered Medline: 12 Jan 1999

AB Lysophosphatidic acid (LPA), plasmalogen-glycerophosphate (alkenyl-GP) and, cyclic-phosphatidic acid (cyclic-PA) are naturally occurring phospholipid growth factors (PLGFs). PLGFs elicit diverse biological effects via the activation of G protein-coupled receptors in a variety of cell types. In NIH3T3 fibroblasts, LPA and alkenyl-GP both induced proliferation, whereas cyclic-PA was antiproliferative. LPA and alkenyl-GP decreased cAMP in a pertussis toxin-sensitive manner, whereas cyclic-PA caused cAMP to increase. LPA and alkenyl-GP both stimulated the activity of the mitogen-actived protein kinases extracellular signal regulated kinases 1 and 2 and c-Jun NH2-terminal kinase, whereas cyclic-PA did not. All three PLGFs induced the formation of stress fibers in NIH3T3 fibroblasts. To determine whether these lipids activated the same or different receptors, heterologous desensitization patterns were established among the three PLGFs by monitoring changes in intracellular Ca2+ in NIH3T3 fibroblasts. LPA cross-desensitized both the alkenyl-GP and cyclic-PA responses. Alkenyl-GP cross-desensitized the cyclic-PA response, but only partially desensitized the LPA response. Cyclic-PA only partially desensitized both the alkenyl-GP and LPA responses. We propose that pharmacologically distinct subsets of PLGF receptors exist that distinguish between cyclic-PA and alkenyl-GP, but are all activated by LPA. We provide evidence that the PSP24 receptor is selective for LPA and not activated by the other two PLGFs. RT-PCR and Northern blot analysis indicate the co-expression of mRNAs encoding the EDG-2, EDG-4, and PSP24 receptors in a variety of cell lines and tissues. However, the lack of mRNA expression for these three receptors in the LPA-responsive Rat-1 and Sp2-O-Ag14 cells suggests that a number of PLGF receptor subtypes remain unidentified.

L12 ANSWER 17 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:358695 BIOSIS
DOCUMENT NUMBER: PREV200300358695
TITLE: Fatty alcohol phosphates are subtype-selective agonists and antagonists of lysophosphatidic acid receptors.

AUTHOR(S): Virag, Tamas [Reprint Author]; Elrod, Don B.; Liliom, Karoly; Sardar, Vineet M.; Parrill, Abby L.; Yokoyama, Kazuaki; Durgam, Gangadhar; Miller, Duane D.; Tigyi, Gabor J.

CORPORATE SOURCE: Physiology, Univ. of Tennessee, 894 Union Ave., Memphis, TN, 38163, USA
tvirag@physio1.utmem.edu; don.elrod@lynntech.com; liliom@enzim.hu; vmsardar@yahoo.com; aparrill@memphis.edu; yokoyama@physio1.utmem.edu; gdurgam@utmem.edu; dmiller@utmem.edu; gtigyi@physio1.utmem.edu

SOURCE: FASEB Journal, (March 2003) Vol. 17, No. 4-5, pp. Abstract No. 123.8. http://www.fasebj.org/. e-file.
Meeting Info.: FASEB Meeting on Experimental Biology: Translating the Genome. San Diego, CA, USA. April 11-15, 2003. FASEB.
ISSN: 0892-6638 (ISSN print).

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 6 Aug 2003
Last Updated on STN: 6 Aug 2003

AB Lysophosphatidic acid (LPA) activates the GPCRs LPA1, LPA2, and LPA3. A better understanding of the physiological and pathological role of LPA requires receptor subtype-specific ligands. Here, we report the synthesis and pharmacological characterization of fatty alcohol phosphates (FAPs) with saturated hydrocarbon chains, ranging from 4 to 22 carbon atoms. Selection of FAP as the lead structure was based on computational modeling as a predicted minimal structure that satisfies the two point pharmacophore model developed earlier. The 10 and 12 carbon chain FAPs (FAP 10 and FAP 12) were found to be specific agonists for LPA2, whilst selective antagonists for LPA3. FAP-12 was a weak antagonist for LPA1. Neither LPA1 nor LPA3 were activated by FAPs , whereas LPA2 was activated by C10-to-14 FAPs. Computational docking FAP 10 and 12 positioned these ligands in the LPA binding pocket in the LPA2 model. The inhibitory effect of FAP showed a strong dependence on the hydrocarbon chain length with C12 being the best in Xenopus oocytes and in LPA3-expressing RH7777 cells. FAP-12 did not activate or interfere with many GPCRs. These data suggest that FAPs are ligands of LPA receptors and that FAP 10 and FAP 12 are the first receptor subtype-specific agonists for LPA2.

L12 ANSWER 21 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:308725 BIOSIS

DOCUMENT NUMBER: PREV200200308725

TITLE: LPA analogs as agonists of the Edg2 LPA receptor.

AUTHOR(S): Erickson, James R. [Inventor, Reprint author]

CORPORATE SOURCE: El Cerrito, CA, USA
ASSIGNEE: Atairgin Technologies, Inc.

PATENT INFORMATION: US 6380177 20020430

SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Apr. 30, 2002) Vol. 1257, No. 5. http://www.uspto.gov/web/menu/patdata.html. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent

LANGUAGE: English

ENTRY DATE: Entered STN: 22 May 2002
Last Updated on STN: 22 May 2002

AB Applicant has probed the Edg2 lysophosphatidic acid (LPA) receptor with a series of LPA analogs to determine receptor activation. The present invention is drawn to a series of LPA analogs which function as Edg2 receptor agonists, and methods of using such compounds to activate the Edg2 receptor of the surface of a cell. The compounds of the invention comprise a glycerol backbone with an Sn1 ester-linked saturated or unsaturated alkyl group,

substitutions of the hydroxyl group (--OH) at carbon two of the glycerol backbone, and optional replacement of the phosphate di-anion with either a hydroxyl group or a dimethylated phosphate. These LPA analogs may find uses in cancer and neurological disorders.

L12 ANSWER 22 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:93755 BIOSIS
DOCUMENT NUMBER: PREV200200093755
TITLE: Agonist-induced internalization of lysophosphatidic acid-coupled Edg2 receptors via clathrin-dependent endocytosis.
AUTHOR(S): Murph, Mandi Michelle [Reprint author]; Scaccia, Launa [Reprint author]; Radhakrishna, Harish [Reprint author]
CORPORATE SOURCE: Biology, Georgia Institute of Technology, 315 First Drive, IBB No. 2228, Atlanta, GA, 30332, USA
SOURCE: Molecular Biology of the Cell, (Nov, 2001) Vol. 12, No. Supplement, pp. 89a. print.
Meeting Info.: 41st Annual Meeting of the American Society for Cell Biology. Washington DC, USA. December 08-12, 2001. American Society for Cell Biology.
CODEN: MBCEEV. ISSN: 1059-1524.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Jan 2002
Last Updated on STN: 25 Feb 2002

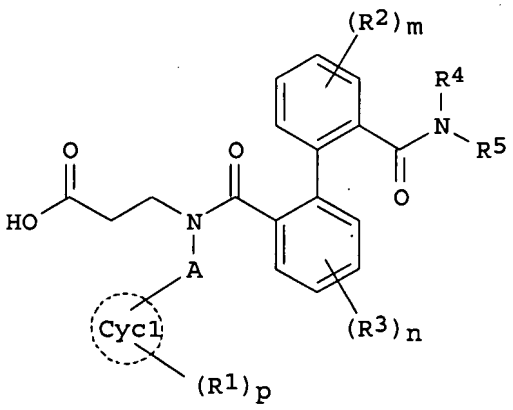
L12 ANSWER 23 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:950976 CAPLUS
DOCUMENT NUMBER: 140:16961
TITLE: Preparation of N-(2'-carbamoyl-1,1'-biphenyl-2-ylcarbonyl)-β-alanine derivatives as lysophosphatidic acid receptor antagonists
INVENTOR(S): Habashita, Hiromu; Terakado, Masahiko; Nakade, Shinji; Seko, Takuya
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 434 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003099765	A1	20031204	WO 2003-JP6678	20030528 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003241833	A1	20031212	AU 2003-241833	20030528
EP 1533294	A1	20050525	EP 2003-733129	20030528
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005256160	A1	20051117	US 2004-515653	20041124
PRIORITY APPLN. INFO.:			JP 2002-153592 A	20020528
			WO 2003-JP6678 W	20030528

OTHER SOURCE(S): MARPAT 140:16961

GI



I

AB The title compds. [I; A = C1-6 alkylene, C2-6 alkenylene, or C2-6 alkynylene each optionally substituted by 1-3 C1-4 alkyl group(s); the ring Cyc1 = C3-15 carbocyclic or 3- to 13-membered heterocyclic ring containing 1-4 N, 1-2 O, and/or 1-2 S atom(s); R1 = C1-4 alkyl, halo, cyano, trihalomethyl, OR6, SR7, NR8R9, NO2, CO2R10, CONR11R12, NR13COR14, SO2NR15R16, NR17SO2R18, S(O)R19, SO2R20; R6-R20 = H, C1-4 alkyl; R2, R3 = C1-4 alkyl, C1-4 alkoxy, halo; R4, R5 = H, C1-4 alkyl, C2-4 alkenyl, C2-4 alkynyl, R21O-C1-4 alkyl, R22R23N-C1-4 alkyl, etc.; or NR4R5 is combined together to represent 3- to 15-membered mono-, di-, or tricyclic heterocyclyl containing at least one N atom and optionally substituted by OR25; wherein R21, R22, R23, R25 = H, C1-4 alkyl, C2-6 acyl, trihaloacetyl; wherein m, n = an integer of 0-4; p = an integer of 0-5; when p, m, or n is ≥2, R1, R2, or R3 is same or different] or prodrugs or salts thereof are prepared These compds. engage in lysophosphatidic acid (LPA) receptor bonding, in particular EDG-2 and antagonism and hence are useful in the prevention and/or treatment of urol. diseases (symptoms associated with prostate-gland enlargement or neuropathic bladder, bone tumors of the spine, disk herniation, spinal canal stenosis, symptoms attributed to diabetes, lower urinary tract infections (e.g., obstruction of lower urinary tract), inflammation of lower urinary tract and polyuria), cancer-associated diseases (solid tumor, solid tumor metastasis, angiofibroma, myeloma, multiple myeloma, Kaposi's sarcoma, leukemia and wet metastasis of cancer), proliferative diseases (diseases accompanied by abnormal angiogenesis, blocked artery and lung fibrosis), inflammation/immune diseases (psoriasis, nephropathy, hepatitis and pneumonia), diseases caused by secretion disorder (Sjogren's syndrome) or brain-associated diseases (brain block, cerebral hemorrhage and cerebral or peripheral nerve disorder). Thus, 3-[N-[2-(2-carboxyphenyl)phenyl]-N-[2-(2,5-dimethoxyphenyl)ethyl]amino]propanoic acid-bound to Wang resin (preparation given) was condensed with 4-chlorobenzylamine using 1-hydroxybenzotriazole monohydrate and N,N-diisopropylcarbodiimide in DMF at room temperature for 16 h, followed by treatment with a 9:1 mixture of CF3CO2H and H2O at room temperature for 1 h to give 3-[N-[2-[2-[(4-chlorobenzylamine)carbonyl]phenyl]carbonyl]-N-[2-(2,5-dimethoxyphenyl)ethyl]amino]propanoic acid (II). In an EDG-2 antagonism assay, II showed IC50 of 0.41 μmol/L for inhibiting the increase in cellular calcium ion-concentration in CHO cells over-expressing human EDG-2 gene. A tablet and an ampule containing II were prepared

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 24 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:532340 CAPLUS
DOCUMENT NUMBER: 139:95489
TITLE: Lysophosphatidic acid (LPA) receptor agonists and antagonists, their preparation, and methods of use
INVENTOR(S): Miller, Duane D.; Tigyi, Gabor; Dalton, James T.; Sardar, Vineet M.; Elrod, Don B.; Xu, Huiping; Baker, Daniel L.; Wang, Dean; Liliom, Karoly; Fischer, David J.; Virag, Tamas; Nusser, Nora
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 73 pp., Cont.-in-part of U.S. Ser. No. 811,838.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003130237	A1	20030710	US 2001-953686	20010917 <--
US 2003027800	A1	20030206	US 2001-811838	20010319 <--
US 6875757	B2	20050405		
CA 2460319	A1	20030327	CA 2002-2460319	20020917 <--
WO 2003024402	A2	20030327	WO 2002-US29593	20020917 <--
WO 2003024402	A3	20040219		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002336595	A1	20030401	AU 2002-336595	20020917 <--
EP 1427424	A2	20040616	EP 2002-773455	20020917
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005508319	T	20050331	JP 2003-528500	20020917
US 2005261252	A1	20051124	US 2005-67884	20050228

PRIORITY APPLN. INFO.:		
US 2000-190370P	P	20000317
US 2001-811838	A2	20010319
US 2001-953686	A	20010917
WO 2002-US29593	W	20020917

OTHER SOURCE(S): MARPAT 139:95489

AB The invention discloses LPA receptor ligand compds. X1C(Q1)CH(X3)C(Q2)X2 [≥1 X1-X3 = (HO)2POZ1 or (HO)2POZ2P(OH)OZ1, X1 and X2 linked together as OPO(OH)O, or X1 and X3 linked together as OPO(OH)NH; ≥1 X1-X3 = R1Y1A with each being the same or different when two of X1-X3 are R1Y1A, or X2 and X3 linked together as N(H)C(O)N(R1); optionally, one of X1-X3 = H; A = direct link, (CH2)k (k = 0-30), O; Y1 = (CH2)l (l = 1-30), O, C(O), S, NR2; Z1 = (CH2)m, O(CH2)m (m = 1- 50), C(R3)H, NH, O, S; Z2 = (CH2)N or (CH2)n (n = 1-50), O; Q1, Q2 = H2, :NR4, :O, combination of H and NR5R6; R1 (for each of X1-X3) = H, (un)branched C1-30 alkyl, (un)branched C2-30 alkenyl, (un)substituted (hetero)aromatic ring, etc.; R2-R8 = H, (un)branched C1-30 alkyl, (un)branched C2-30 alkenyl, etc.], as well as pharmaceutical compns. which include those compds. Also disclosed are methods of using such compds., which have activity as agonists or as antagonists of LPA receptors, the methods including inhibiting LPA activity on an LPA receptor, modulating LPA receptor activity, treating cancer, enhancing cell proliferation, treating a wound, treating apoptosis

or preserving or restoring function in a cell, tissue, or organ, culturing cells, preserving organ or tissue function, and treating a dermatol. condition.

L12 ANSWER 26 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:242130 CAPLUS
DOCUMENT NUMBER: 138:265691
TITLE: Lysophosphatidic acid (LPA) receptor agonists and antagonists, their preparation, and methods of use
INVENTOR(S): Miller, Duane D.; Tigyi, Gabor; Dalton, James T.; Sardar, Vineet M.; Elrod, Don B.; Xu, Huiping; Baker, Daniel L.; Wang, Dean; Liliom, Karoly; Fischer, David J.; Virag, Tamas; Nusser, Nora
PATENT ASSIGNEE(S): The University of Tennessee Research Corporation, USA
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024402	A2	20030327	WO 2002-US29593	20020917 <--
WO 2003024402	A3	20040219		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003130237	A1	20030710	US 2001-953686	20010917 <--
CA 2460319	A1	20030327	CA 2002-2460319	20020917 <--
AU 2002336595	A1	20030401	AU 2002-336595	20020917 <--
EP 1427424	A2	20040616	EP 2002-773455	20020917
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005508319	T	20050331	JP 2003-528500	20020917

PRIORITY APPLN. INFO.:

US 2001-953686	A	20010917
US 2000-190370P	P	20000317
US 2001-811838	A2	20010319
WO 2002-US29593	W	20020917

OTHER SOURCE(S): MARPAT 138:265691
AB The invention discloses LPA receptor agonists and antagonists, as well as pharmaceutical compns. which include those compds. Compound preparation is described. Also disclosed are methods of using the compds., such methods including inhibiting LPA activity on an LPA receptor, modulating LPA receptor activity, treating cancer, enhancing cell proliferation, treating a wound, treating apoptosis or preserving or restoring function in a cell, tissue, or organ, culturing cells, preserving organ or tissue function, and treating a dermatol. condition.

L12 ANSWER 27 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:184214 CAPLUS
TITLE: Synthesis and biological evaluation of lysophosphatidic acid antagonists
AUTHOR(S): Heasley, Brian H.; Macdonald, Timothy L.; Lynch, Kevin R.
CORPORATE SOURCE: Department of Chemistry, University of Virginia,

Charlottesville, VA, 22904-4319, USA
SOURCE: Abstracts of Papers, 225th ACS National Meeting, New Orleans, LA, United States, March 23-27, 2003 (2003), MEDI-248. American Chemical Society: Washington, D. C.
CODEN: 69DSA4
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Lysophosphatidic acid (LPA) antagonists have potential applications as inhibitors of inflammation, cancer invasiveness, and atherogenesis. However, the detailed physiol. implications of LPA occupancy of individual receptors are largely unknown because subtype-selective agonists/antagonists are unavailable currently. Compds. containing bulky hydrophobic substituents at the 2-position of an N-acyl ethanolamide phosphate core structure have been shown to possess dual LPA1/LPA3 competitive antagonism. The most potent analog of this series (VPC12249) has been modified so as to optimize potency and selectivity at LPA receptors. Compds. containing variation in the acyl chain, linker region, and polar head group have been synthesized and screened for biol. activity at LPA receptors. Several dual antagonists of comparable activity have been discovered. One compound (VPC32104) shows improved potency and selectivity for LPA1. This paper will describe the sythetic methods and biol. evaluation of LPA receptor antagonists.

L12 ANSWER 29 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:276112 CAPLUS
DOCUMENT NUMBER: 136:289091
TITLE: Novel lysophosphatidic acid receptor agonists and antagonists
INVENTOR(S): Lynch, Kevin R.; MacDonald, Timothy L.; Heise, Christopher E.; Santos, Webster L.; Okusa, Mark D.
PATENT ASSIGNEE(S): University of Virginia Patent Foundation, USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002029001	A2	20020411	WO 2001-US30936	20011003 <--
WO 2002029001	A3	20030821		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 200196536	A	20020415	AU 2001-96536	20011003 <--
EP 1361872	A2	20031119	EP 2001-977415	20011003 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004122236	A1	20040624	US 2003-398305	20031015
US 7169818	B2	20070130		

PRIORITY APPLN. INFO.:	US 2000-237436P	P 20001003
	US 2001-264046P	P 20010125
	US 2001-297507P	P 20010613
	WO 2001-US30936	W 20011003

OTHER SOURCE(S): MARPAT 136:289091
AB The present invention is directed to compns. comprising

lysophosphatidic acid analogs and methods of using such analogs as agonist or antagonists of lysophosphatidic acid (LPA) receptor activity. In addition the invention is directed to LPA receptor agonists that vary in the degree of selectivity at individual LPA receptors (i.e. LPA1, LPA2 and LPA3). More particularly the present invention is directed to LPA analogs wherein the glycerol is replaced with ethanolamine and a variety of substitutions have been linked at the second carbon atom.

L12 ANSWER 31 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:713600 CAPLUS
DOCUMENT NUMBER: 135:267219
TITLE: Synthesis of lysophosphatidic acid receptor agonists and antagonists and their use for cancer inhibition, wound healing, and enhancement of cell proliferation
INVENTOR(S): Miller, Duane D.; Tigyi, Gabor; Dalton, James T.; Sardar, Vineet M.; Elrod, Don B.; Xu, Huiping; Baker, Daniel L.; Wang, Dean; Liliom, Karoly; Fischer, David J.; Virag, Tamas; Nusser, Nora
PATENT ASSIGNEE(S): University of Tennessee Research Corporation, USA
SOURCE: PCT Int. Appl., 140 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001071022	A2	20010927	WO 2001-US8729	20010319 <--
WO 2001071022	A3	20020404		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2402038	A1	20010927	CA 2001-2402038	20010319 <--
AU 200149263	A	20011003	AU 2001-49263	20010319 <--
EP 1263752	A2	20021211	EP 2001-922465	20010319 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004506604	T	20040304	JP 2001-569403	20010319
PRIORITY APPLN. INFO.:			US 2000-190370P P	20000317
			WO 2001-US8729 W	20010319

OTHER SOURCE(S): MARPAT 135:267219

AB The present invention relates to lysophosphatidic acid (LPA) analogs and cyclic derivs. of the analogs as well as pharmaceutical compns. which include those compds. Also disclosed are methods of using such compds., which have activity as agonists or as antagonists of LPA receptors; such methods including inhibiting LPA activity on an LPA receptor, modulating LPA receptor activity, treating cancer, enhancing cell proliferation, and treating a wound. Thus, 2-amino-3-oxo-3-(tetradecylamino)propyl dihydrogen phosphate (I), 2-(acetylamino)-3-oxo-3-(tetradecylamino)propyl dihydrogen phosphate (II), and 1,2-(3-octadecyloxypropane)-bis(dihydrogen phosphate) (III) were synthesized. The cytotoxicity of these compds. on prostate cancer cell lines was determined The IC50's observed were 0.7 ± 0.1 for I on PC-3 cells, 0.7 ± 0.1 for II on DU145 cells, and 3.1 ± 3.2 for III on LNCaP cells. Addnl., phosphoric acid monododecyl ester (IV) was prepared and screened in Xenopus oocytes (which produce the PSP24 receptor) and in

recombinant RH7777 cells producing Edg-2, Edg-4, and Edg-7 receptors. In Xenopus IV inhibited LPA-induced chloride currents with an IC50 value of about 8.1 nM. In Edg-2 and Edg-4-expressing RH7777 cells IV significantly inhibited the Ca2+ responses while in Edg-7-expressing cells this compound increased the Ca2+ responses.

L12 ANSWER 32 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:688874 CAPLUS
DOCUMENT NUMBER: 135:341872
TITLE: Assessment of agonism at G-protein coupled receptors by phosphatidic acid and lysophosphatidic acid in human embryonic kidney 293 cells
AUTHOR(S): Alderton, Forbes; Sambi, Balwinder; Tate, Rothwelle; Pyne, Nigel J.; Pyne, Susan
CORPORATE SOURCE: Department of Physiology and Pharmacology, Strathclyde Institute for Biomedical Sciences, University of Strathclyde, Glasgow, G4 0NR, UK
SOURCE: British Journal of Pharmacology (2001), 134(1), 6-9
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several different mol. species of phosphatidic acid (PA) bind to a G-protein coupled receptor (GPCR) to induce activation of the p42/p44 mitogen-activated protein kinase (p42/p44 MAPK) pathway in HEK 293 cells. PA is active at low nanomolar concns. and the response is sensitive to pertussis toxin (which uncouples GPCRs from Gi/o). The de-acylated product of PA, lysophosphatidic acid (LPA), which binds to members of the endothelial differentiation gene (EDG) family of receptors also stimulated p42/p44 MAPK in a pertussis toxin sensitive manner, but with an .apprx. 100-1000 fold lower potency compared with the different mol. species of PA. RT-PCR using gene-specific primers showed that HEK 293 cells express EDG2 and PSP24, the latter being a lipid binding GPCR out with the EDG cluster. We conclude that PA is a novel high potency GPCR agonist.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> Log Off H
SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 11:25:59 ON 03 JUL 2007

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAEGS1646

PASSWORD:
* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'STNGUIDE' AT 12:59:51 ON 03 JUL 2007
FILE 'STNGUIDE' ENTERED AT 12:59:51 ON 03 JUL 2007
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.06	103.09

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION

```
CA SUBSCRIBER PRICE                                    0.00       -8.58

=> D Hist

     (FILE 'HOME' ENTERED AT 09:45:37 ON 03 JUL 2007)

     FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 09:45:58 ON 03 JUL 2007
L1        108930 S NEPHROPATHY
L2         10068 S LYSOPHOSPHATIDIC ACID
L3           419 S EDG RECEPTOR
L4             0 S L1 AND L2 AND L3
L5           190 S L2 AND L3
L6            87 DUP REM L5 (103 DUPLICATES REMOVED)
L7             4 S L6 AND THERAPY
L8             4 S L6 AND MODULATOR
L9          1072 S L2 (S)(AGONIST OR ANALOG OR ANTAGONIST OR INHIBITOR)
L10          695 S L9 AND PD<=20031211
L11          303 DUP REM L10 (392 DUPLICATES REMOVED)
L12           37 S L11 (S)(EDG-2 OR EDG2 OR LPA1)

     FILE 'STNGUIDE' ENTERED AT 11:23:39 ON 03 JUL 2007

     FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 11:25:48 ON 03 JUL 2007

     FILE 'STNGUIDE' ENTERED AT 11:25:50 ON 03 JUL 2007

=> S L3(S)(Endogenous(W)Expression)
             0 EDG
             0 RECEPTOR
             0 EDG RECEPTOR
                 (EDG(W)RECEPTOR)
             0 ENDOGENOUS
             2 EXPRESSION
L13          0 L3(S)(ENDOGENOUS(W)EXPRESSION)

=> S L3 AND (Endogenous(W)Expression)
             0 EDG
             0 RECEPTOR
             0 EDG RECEPTOR
                 (EDG(W)RECEPTOR)
             0 ENDOGENOUS
             2 EXPRESSION
             0 ENDOGENOUS(W)EXPRESSION
L14          0 L3 AND (ENDOGENOUS(W)EXPRESSION)

=> S L3 AND Expression
             0 EDG
             0 RECEPTOR
             0 EDG RECEPTOR
                 (EDG(W)RECEPTOR)
             2 EXPRESSION
L15          0 L3 AND EXPRESSION

=> S L3 AND Cell
             0 EDG
             0 RECEPTOR
             0 EDG RECEPTOR
                 (EDG(W)RECEPTOR)
            15 CELL
L16          0 L3 AND CELL

=> S L2(W)receptor
             0 LYSOPHOSPHATIDIC
             6 ACID
             1 ACIDS
```

```
            6 ACID
                (ACID OR ACIDS)
            0 LYSOPHOSPHATIDIC ACID
                (LYSOPHOSPHATIDIC(W)ACID)
            0 RECEPTOR
L17         0 L2(W)RECEPTOR

=> File .gerry2MBCE
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.48     103.51

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00      -8.58

FILE 'MEDLINE' ENTERED AT 13:04:48 ON 03 JUL 2007

FILE 'BIOSIS' ENTERED AT 13:04:48 ON 03 JUL 2007
Copyright (c) 2007 The Thomson Corporation

FILE 'CAPLUS' ENTERED AT 13:04:48 ON 03 JUL 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'EMBASE' ENTERED AT 13:04:48 ON 03 JUL 2007
Copyright (c) 2007 Elsevier B.V. All rights reserved.

=> S L3(S)(Endogenous(W)Expression)
L18         0 L3(S)(ENDOGENOUS(W) EXPRESSION)

=> S L3 AND (Endogenous(W)Expression)
L19         0 L3 AND (ENDOGENOUS(W) EXPRESSION)

=> S L3 AND Expression
L20       196 L3 AND EXPRESSION

=> S L20 S Kidney
MISSING OPERATOR L20 S KIDNEY
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> S l20(S)kidney
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L80(S)KIDNEY'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L81(S)KIDNEY'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L82(S)KIDNEY'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L83(S)KIDNEY'
L21         3 L20(S) KIDNEY

=> D abs L21 1-3

L21  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2007 ACS on STN
AB   Lysophosphatidic acid (LPA), a major member of the bioactive
     lysophospholipids in serum, possesses diverse physiol. activities
     including cell proliferation.  Recently, three endothelial differentiation
     gene (EDG) family receptors, including EDG-2 (LPA1), EDG-4 (LPA2), and
     EDG-7 (LPA3), have been identified as LPA receptors.  The role of LPA and
     their receptors in mesangial cell physiol. is not clearly understood.
     This study examined the expression profile of EDG
     receptors as a function of cell d. and the participation of
```

EDG receptors in human mesangial cell proliferation by LPA. We showed that mesangial cells express all three EDG family LPA receptors in a cell d.-dependent manner. EDG-7 maximally expressed at sparse cell d. and minimally expressed in dense cell population. The EDG-2 expression pattern was opposite to the EDG-7. No changes in EDG-4 expression as a function of cell d. were noted. DNA synthetic rate was greater in sparse cell d. compared with dense cell population and followed a similar pattern with EDG-7 expression. Comparative studies in sparse and dense cell d. indicated that EDG-7 was pos. associated, whereas EDG-2 was neg. associated with cell proliferation rate.

LPA induced mesangial cell proliferation by 1.5- to 3.5-fold. Dioctanoylglycerol pyrophosphate, an antagonist for EDG-7, almost completely inhibited mesangial cell proliferation induced by LPA. We suggest that EDG-7 regulates LPA-mediated mesangial cell proliferation. Addnl., these data suggest that EDG-7 and EDG-2 LPA receptors play a diverse role as proliferative and antiproliferative, resp., in mesangial cells. Regulation of EDG family receptors may be importantly linked to mesangial cell-proliferative processes.

L21 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN

AB RGS proteins finely tune heterotrimeric G-protein signaling. Implying the need for such fine-tuning in the developing vascular system, in situ hybridization revealed a striking and extensive expression pattern of Rgs5 in the arterial walls of E12.5-E17.5 mouse embryos. The distribution and location of the Rgs5-pos. cells typified that of pericytes and strikingly overlapped the known expression pattern of platelet-derived growth factor receptor (PDGFR)-β. Both E14.5 PDGFR-β- and platelet-derived growth factor (PDGF)-B-deficient mice exhibited markedly reduced levels of Rgs5 in their vascular plexa and small arteries. This likely reflects the loss of pericytes in the mutant mice. RGS5 acts as a potent GTPase activating protein for Giα and Gqα and it attenuated angiotensin II-, endothelin-1-, sphingosine-1-phosphate-, and PDGF-induced ERK-2 phosphorylation. Together these results indicate that RGS5 exerts control over PDGFR-β and GPCR-mediated signaling pathways active during fetal vascular maturation.

L21 ANSWER 3 OF 3 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

AB Recently, a family of G-protein-coupled receptors named endothelial differentiation gene (Edg) receptor family has been identified, which are specifically activated by the two serum lipids, sphingosine-1-phosphate and lysophosphatidic acid. Sphingosine-1-phosphate can also act intracellularly to release Ca(2+) from intracellular stores. Since in several cell types, G-protein-coupled lysophosphatidic acid or sphingosine-1-phosphate receptors mobilize Ca(2+) in the absence of a measurable phospholipase C stimulation, it was analysed here whether intracellular sphingosine-1-phosphate production was the signalling mechanism used by extracellular sphingosine-1-phosphate for mobilization of stored Ca(2+). Sphingosine-1-phosphate and the low affinity sphingosine-1-phosphate receptor agonist, sphingosylphosphorylcholine, induced a rapid, transient and nearly complete pertussis toxin-sensitive Ca(2+) mobilization in human embryonic kidney (HEK-293) cells. The G-protein-coupled sphingosine-1-phosphate receptors, Edg-1, Edg-3 and Edg-5, were found to be endogenously expressed in these cells. Most interestingly, sphingosine-1-phosphate and sphingosylphosphorylcholine did not induce a measurable production of inositol-1,4,5-trisphosphate or accumulation of inositol phosphates. Instead, sphingosine-1-phosphate and sphingosylphosphorylcholine induced a rapid and transient increase in production of intracellular sphingosine-1-phosphate with a maximum of about 1.4-fold at 30 s. Stimulation of sphingosine-1-phosphate formation by sphingosine-1-phosphate and sphingosylphosphorylcholine was fully blocked by pertussis toxin, indicating that extracellular

sphingosine-1-phosphate via endogenously expressed G(i)-coupled receptors induces a stimulation of intracellular sphingosine-1-phosphate production. As sphingosine-1-phosphate- and sphingosylphosphorylcholine-induced increases in intracellular Ca(2+) were blunted by sphingosine kinase inhibitors, this sphingosine-1-phosphate production appears to mediate Ca(2+) signalling by extracellular sphingosine-1-phosphate and sphingosylphosphorylcholine in HEK-293 cells. .COPYRGT. 2001 Elsevier Science B.V.

=> D ibib l21 1-3

L21 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1075963 CAPLUS
DOCUMENT NUMBER: 142:20821
TITLE: Cell density-dependent expression of EDG family receptors and mesangial cell proliferation: Role in lysophosphatidic acid-mediated cell growth
AUTHOR(S): Xing, Yiding; Ganji, Shobha H.; Noh, Jung W.; Kamanna, Vaijinath S.
CORPORATE SOURCE: Medical Research Service, Department of Veterans Affairs Healthcare System, Long Beach, 90822, USA
SOURCE: American Journal of Physiology (2004), 287(6, Pt. 2), F1250-F1257
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:212940 CAPLUS
DOCUMENT NUMBER: 139:1403
TITLE: Pericyte-specific expression of RGS5: implications for PDGF and EDG receptor signaling during vascular maturation
AUTHOR(S): Cho, Hyeseon; Kozasa, Tohru; Bondjers, Cecilia; Betsholtz, Christer; Kehrl, John H.
CORPORATE SOURCE: National Institute of Allergy and Infectious Diseases, Lab. of Immunoregulation, National Institute of Allergy and Infectious Diseases, Bethesda, MD, 20892-1876, USA
SOURCE: FASEB Journal (2003), 17(3), 440-442, 10.1096/fj.02-0340fje
CODEN: FAJOEC; ISSN: 0892-6638
PUBLISHER: Federation of American Societies for Experimental Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 3 OF 3 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2001084181 EMBASE
TITLE: Stimulation of intracellular sphingosine-1-phosphate production by G-protein-coupled sphingosine-1-phosphate receptors.
AUTHOR: Meyer zu Heringdorf D.; Lass H.; Kuchar I.; Lipinski M.; Alemany R.; Rumenapp U.; Jakobs K.H.
CORPORATE SOURCE: D. Meyer zu Heringdorf, Institut fur Pharmakologie, Universitatsklinikum Essen, Hufelandstrasse 55, D-45122 Essen, Germany. meyer-heringdorf@uni-essen.de
SOURCE: European Journal of Pharmacology, (2 Mar 2001) Vol. 414,

No. 2-3, pp. 145-154. .
Refs: 36
ISSN: 0014-2999 CODEN: EJPHAZ
PUBLISHER IDENT.: S 0014-2999(01)00789-0
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 6 Apr 2001
Last Updated on STN: 6 Apr 2001

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	29.56	133.07

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.56	-10.14

FILE 'STNGUIDE' ENTERED AT 13:09:13 ON 03 JUL 2007

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Jun 29, 2007 (20070629/UP).

=> Log off h
SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 13:16:20 ON 03 JUL 2007